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# TRANSMITTAL FORM

*(to be used for all correspondence after initial filing)*

Total Number of Pages in This Submission: 18

| | |
|---|---|
| Application Number | 10/700,971 |
| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
| Attorney Docket Number | CHEM0005US.P1 (ISIC0009-101) |

## ENCLOSURES *(Check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☑ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☑ Other Enclosure(s) (please Identify below):

Forms PTO/SB/08a and PTO/SB/08b (13pp.); Copies of (110) References Cited Enclosed.

Remarks

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | | | |
|---|---|---|---|
| Firm Name | Isis Pharmaceuticals, Inc. | | |
| Signature | Robert S. Andrews | | |
| Printed name | Robert S. Andrews | | |
| Date | January 17, 2005 | Reg. No. | 44,508 |

## CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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|---|---|---|---|
| Signature | Kemlyn Evans | | |
| Typed or printed name | Kemlyn Evans | Date | January 17, 2005 |

| | |
|---|---|
| APPLICATION NUMBER: | **10/700,971** |
| FILING DATE: | **November 4, 2003** |
| FIRST NAMED INVENTOR: | **Muthiah Manoharan** |
| ART UNIT: | **1623** |
| EXAMINER NAME: | **To Be Determined** |
| ATTORNEY DOCKET NUMBER: | **CHEM0005US.P1 (ISIC0009-101)** |
| TITLE: | **CONJUGATED OLIGOMERIC COMPOUNDS AND THEIR USE IN GENE MODULATION** |

I certify that this communication is being deposited with the U.S. Postal Service in an envelope addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 utilizing the "Express Mail Post Office to Addresses" service under Mailing Label No. EL071214675US on the date shown below:

Dated: 1-17-05 By: Robert S. Andrews

Robert S. Andrews, Reg. No.44,508

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INFORMATION DISCLOSURE STATEMENT
Under 37 C.F.R. §§ 1.56 and 1.97-98

SIR:

Pursuant to the provisions of 37 C.F.R. §§ 1.56 and 1.97-98, enclosed herewith is PTO Form PTO/SB/08A and PTO/SB/08B listing references for consideration by the Examiner.

The filing of this Information Disclosure Statement shall not be construed as a representation regarding the completeness of the list of references, or that inclusion of a reference in this list is an admission that it is prior art or is pertinent to this application, or that a search has been made, or as an admission that the information listed is, or may be considered to be, material to patentability, or that no other material information exists, and shall not be construed as an admission against interest in any manner.

This Information Disclosure Statement is being filed:

☒ within three months of the filing date of the application, or date of entry into the national stage of an international application, or before the mailing date of a first office action on the merits, whichever event last occurred;

☐ before the mailing of a first official action after filing of a request for continued examination (RCE) under 37 C.F.R. § 1.114;

☐ after three months of the filing date of this national application or the date of entry of the national stage in an international application, or after the mailing date of the first official action on the merits, whichever event last occurred, but before that mailing date of the first office action to occur of either: (1) a final action under 37 C.F.R. § 1.113; or (2) an action that otherwise closes prosecution in the application, and:

☐ attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR

☐ Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

☐ each item of the information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement;

OR

☐ no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement.

☐ on or before the payment of the issue fee but after the mailing date of the first to occur of either: (1) a final action under 37 C.F.R. § 1.113; (2) a notice of allowance under 37 C.F.R. § 1.311; or (3) an action that otherwise closes prosecution in the application, and:

☐ Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

☐ each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement;

OR

☐ no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement. AND

☐ attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR

☐ after the payment of the issue fee. Applicant requests that the information contained in this Information Disclosure Statement be placed in the file according to 37 C.F.R. § 1.97(i), although the information may not be considered by the USPTO.

☒ Enclosed is a copy of each listed reference that may be material to the examination of this application, and for which there may be a duty to disclose.

☐ This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior application No. , filed on , and the references cited therein are herby referenced, but are not required to be provided in this application under 37 C.F.R. § 1.98(d).

☒ This application was filed after June 30, 2003. Therefore, pursuant to the waiver of the requirements under 37 C.F.R. § 1.98(a)(2)(i), copies of each U.S. Patent and each U.S. Patent Application Publication are not required to be submitted. Copies of any foreign patent documents and non-patent literature cited herein are enclosed.

☐ Each item of information contained in this Information Disclosure Statement was cited in the communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this Information Disclosure Statement 37 C.F.R. § 1.704(d).

☒ Applicant submits that no fee is required for the consideration of this Information Disclosure Statement.

Consideration of the listed references and favorable action are solicited.

Respectively Submitted,

Robert S. Andrews Dated: 1-17-05

Robert S. Andrews
Registration No.: 44,508
Isis Pharmaceuticals, Inc.
2292 Faraday Ave.
Carlsbad, CA 92008

PTO/SB/08a (08-03)
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

*(Use as many sheets as necessary)*

Sheet 1 of 13

| Complete if Known | |
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| Application Number | 10/700,971 |
| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
| Attorney Docket Number | CHEM0005US.P1 (ISIC0009-101) |

## U.S. PATENT DOCUMENTS

| Examiner Initials * | Cite No.[1] | Document Number: Number - Kind Code[2] (*if known*) | Publication/Issue Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
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| Examiner Initials* | Cite No.[1] | Foreign Patent Document: Country Code[3] - Number[4] - Kind Code[5] (*if known*) | Publication Date/Filing Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T[6] |
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| | BC | ✓ WO 01/29058 | 04-26-2001 | Univ. of Mass. | | |

| Examiner Signature | | Date Considered | |
|---|---|---|---|

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

*(Use as many sheets as necessary)*

Sheet 2 of 13

| *Complete if Known* | |
|---|---|
| *Application Number* | 10/700,971 |
| *Filing Date* | November 4, 2003 |
| *First Named Inventor* | Muthiah Manoharan |
| *Art Unit* | 1623 |
| *Examiner Name* | To Be Determined |
| *Attorney Docket Number* | CHEM0005US.P1 (ISIC0009-101) |

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| Examiner Initials* | Cite No.[1] | Foreign Patent Document<br>Country Code[3] - Number[4] - Kind Code[5] (*if known*) | Publication Date/Filing Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T[6] |
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| Examiner Signature | | Date Considered | |
|---|---|---|---|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 13

| *Complete if Known* | |
|---|---|
| *Application Number* | 10/700,971 |
| *Filing Date* | November 4, 2003 |
| *First Named Inventor* | Muthiah Manoharan |
| *Art Unit* | 1623 |
| *Examiner Name* | To Be Determined |
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

*(Use as many sheets as necessary)*

Sheet 4 of 13

| *Complete if Known* | |
|---|---|
| *Application Number* | 10/700,971 |
| *Filing Date* | November 4, 2003 |
| *First Named Inventor* | Muthiah Manoharan |
| *Art Unit* | 1623 |
| *Examiner Name* | To Be Determined |
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| | DM | US-6,444,806 | 09-03-2002 | Veerapaneni | |
| | DN | US-6,486,308 | 11-26-2002 | Kutyavin | |
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| *Examiner Name* | To Be Determined |
| *Attorney Docket Number* | CHEM0005US.P1 (ISIC0009-101) |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials * | Cite No.[1] | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T[2] |
|---|---|---|---|
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| | DT | BAKER, B. F. et al., "Oligonucleotide-europium complex conjugate designed to cleave the 5' cap structure of the ICAM-1 transcript potentiates antisense activity in cells," *Nucleic Acids Res.* (1999) 27(6):1547-1551. | |
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| | DV | BONGARTZ, J.-P. et al., "Improved biological activity of antisense oligonucleotides conjugated to a fusogenic peptide," *Nucleic Acids Res.* (1994) 22(22):4681-4688. | |
| | DW | BONORA, G. M. et al., "Biological Properties of Antisense Oligonucleotides Conjugated to Different High-Molecular Mass Poly(Ethylen Glycols)," *Nucleosides Nucleotides* (1999) 18(6&7):1723-1725. | |
| | DX | BONORA, G. M. et al., "Antisense activity of an anti-HIV oligonucleotide conjugated to linear and branched high molecular weight polyethylene glycols," *Farmaco* (1998) 53:634-637. | |
| | DY | BOUTLA, A. et al., "Short 5'-phosphorylated double-stranded RNAs induce RNA interference in *Drosphila*," *Curr. Biol.* (2001) 11:1776-1780. | |

| Examiner Signature | | Date Considered | |
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 6 of 13

| Complete if Known | |
|---|---|
| Application Number | 10/700,971 |
| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
| Attorney Docket Number | CHEM0005US.P1 (ISIC0009-101) |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials * | Cite No.[1] | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T[2] |
|---|---|---|---|
| | DZ | BRANDEN, L. J. et al., "A peptide nucleic acid-nuclear localization signal fusion that mediates nuclear transport of DNA," *Nature Biotech* (1999) 17:784-787. | |
| | EA | BRANTL, S., "Antisense-RNA regulation and RNA interference," *Biochimica et Biophysica Acta* (2001) 1575:15-25. | |
| | EB | CAZALLA, D. et al., "Nuclear Export and Retention Signals in the RS Domain of SR Proteins," *Mol. Cell. Biol.* (2002) 22(19):6871-6882. | |
| | EC | CHALOIN, L. et al., "Design of Carrier Peptide-Oligonucleotide Conjugates with Rapid Membrane Translocation and Nuclear Localization Properties," *Biochem. Biophys. Res. Commun.* (1998) 243:601-608. | |
| | ED | CHIANG, M.-Y. et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule I Expression by Two Distinct Mechanisms," *J. Biol. Chem.* (1991) 266(27):18162-18171. | |
| | EE | CHIU, Y.-L. et al., "RNAi in Human Cells: Basic Structural and Functional Features of Small Interfering RNA," *Molecular Cell* (2002) 10:549-561. | |
| | EF | COGONI, C. et al., "Post-transcriptional gene silencing across kingdoms," *Genes Dev.* (2000) 10:638-643. | |
| | EG | COHEN, G. L. et al., "Sequence Dependent Binding of *cis*-Dichlorodiammineplatinum(II) to DNA," *J. Am. Chem. Soc.* (1980) 102(7):2487-2488. | |
| | EH | COREY, D. R., "48000-fold Acceleration of Hybridization by Chemically Modified Oligonucleotides," *J. Am. Chem. Soc.* (1995) 117(36):9373-9374. | |
| | EI | COREY, D. R. et al., "Generation of a Hybrid Sequence-Specific Single-Stranded Deoxyribonuclease," *Science* (1987) 238:1401-1403. | |
| | EJ | COREY, D. R. et al., "Sequence-Selective Hydrolysis of Duplex DNA by an Oligonucleotide-Directed Nuclease," *J. Am. Chem. Soc.* (1989) 111(22):8523-8525. | |

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Sheet 7 of 13

| Complete if Known | |
|---|---|
| Application Number | 10/700,971 |
| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
| Attorney Docket Number | CHEM0005US.P1 (ISIC0009-101) |

**NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials * | Cite No.[1] | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T[2] |
|---|---|---|---|
| | EK | DUFF, R. J. et al., "[17] Intrabody Tissue-Specific Delivery of Antisense Conjugates in Animals: Ligand-Linker-Antisense Oligomer Conjugates," *Methods Eanzymol.* (2000) 313:297-321. | |
| | EL | EFIMOV, V. A. et al., "Synthesis of Polyethylene Glycol - Oligonucleotide Conjugates," *Bioorg. Khim.* (1993) 19(8):800-804. | |
| | EM | ELBASHIR, S. M. et al., "RNA interference is mediated by 21- and 22-nucleotide RNAs," *Genes Dev.* (2001) 15:188-200. | |
| | EN | ELBASHIR, S. M. et al., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," *Nature* (2001) 411:494-498. | |
| | EO | ELBASHIR, S. M. et al., "Functional anatomy of siRNAs for mediating efficient RNAi in *Drosophila melanogaster* embryo lysate," *EMBO J.* (2001) 20(23):6877-6888. | |
| | EP | FIRE, A. et al., "Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*," *Nature* (1998) 391:806-811. | |
| | EQ | FIRESTONE, R. A., "Low-Density Lipoprotein as a Vehicle for Targeting Antitumor Compounds to Cancer Cells," *Bioconjugate Chem.* (1994) 5:105-113. | |
| | ER | GORLACH, M. et al., "The mRNA Poly(A)-Binding Protein: Localization, Abundance, and RNA-Binding Specificity," *Exp. Cells Res.* (1994) 211:400-407. | |
| | ES | GUO, S. et al., "*par-1*, a Gene Required for Establishing Polarity in C. elegans Embryos, Encodes a Putative Ser/Thr Kinase That Is Asymmetrically Distributed," *Cell* (1995) 81:611-620. | |
| | ET | GURA, T., "A silence that speaks volumes," *Nature* (2000) 404:804-808. | |
| | EU | GUZAEV, A. et al., "Conjugation of Oligonucleotides Via an Electrophilic Tether: *N*-Chloroacetamidohexyl Phosphoramidite Reagent," *Bioorg. Med. Chem. Lett.* (1998) 8:3671-3676. | |

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Sheet 8 of 13

| *Complete if Known* | |
|---|---|
| *Application Number* | 10/700,971 |
| *Filing Date* | November 4, 2003 |
| *First Named Inventor* | Muthiah Manoharan |
| *Art Unit* | 1623 |
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| *Attorney Docket Number* | CHEM0005US.P1 (ISIC0009-101) |

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|---|---|---|---|
| | EV | HALL, J. et al., "Efficient sequence-specific cleavage of RNA using novel europium complexes conjugated to oligonucleotides," *Chem. Biol.* (1994) 1(3):185-190. | |
| | EW | HARITON-GAZAL, E. et al., "Targeting of Nonkaryophilic Cell-Permeable Peptides into the Nuclei of Intact Cells by Covalently Attached Nuclear Localization Signals," *Biochemistry* (2002) 41(29):9208-9214. | |
| | EX | HENDERSON, B. R. et al., "A Comparison of the Activity, Sequence Specificity, and CRM1-Dependence of Different Nuclear Export Signals," *Exp. Cell Res.* (2000) 256:213-224. | |
| | EY | HUANG, L. et al., "Oligonucleotide conjugates of Eu(III) tetraazamacrocycles with pendent alcohol and amide groups promote sequence-specific RNA cleavage," *J. Biol. Inorg. Chem.* (2000) 5:85-92. | |
| | EZ | HUH, N. et al., "Design, Synthesis, and Evaluation of Mitomycin-Tethered Phosphorothioate Oligodeoxynucleotides," *Bioconjugate Chem.* (1996) 7:659-669. | |
| | FA | JASCHKE, A. et al., "Synthesis and properties of oligodeoxyribonucleotide-polyethylene glycol conjugates," *Nucleic Acids Res.* (1994) 22(22):4810-4817. | |
| | FB | JORGENSEN, R. A. et al., "Chalcone synthase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense constructs and single-copy vs. complex T-DNA sequences," *Plant Mol. Biol.* (1996) 31:957-973. | |
| | FC | JUBY, C. D. et al., "Facile Preparation of 3'Oligonucleotide-Peptide Conjugates," *Tetrahedron Letters* (1991) 32(7):879-882. | |
| | FD | KABANOV, A. V. et al., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells," *FEBS Lett.* (1990) 259(2):327-330. | |
| | FE | KRIEG, A. M. et al., "Uptake of Oligodeoxyribonucleotides by Lymphoid Cells Is Heterogeneous and Inducible," *Antisense Research and Development* (1991) 1:161-171. | |
| | FF | KUIJPERS, W. H. A. et al., "Specific Recognition of Antibody-Oligonucleotide Conjugates by Radiolabeled Antisense Nucleotides: A Novel Approach for Two-Step Radioimmunotherapy of Cancer," *Bioconjugate Chem.* (1993) 4(1):94-102. | |

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Sheet 9 of 13

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|---|---|
| Application Number | 10/700,971 |
| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
| Attorney Docket Number | CHEM0005US.P1 (ISIC0009-101) |

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| | FG | LETSINGER, R. L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture," *Proc. Natl. Acad. Sci. USA* (1989) 86:6553-6556. | |
| | FH | LI, S. et al., "Folate-Mediated Targeting of Antisense Oligodeoxynucleotides to Ovarian Cancer Cells," *Pharm. Res.* (1998) 15(10):1540-1545. | |
| | FI | LIMA, W. F. et al., "Highly efficient endonucleolytic cleavage of RNA by a $Cys_2His_2$ zinc-finger peptide," *Proc. Natl. Acad. Sci. USA* (1999) 96:10010-10015. | |
| | FJ | LIN, M. et al., "Inhibition of collagenase type I expression by psoralen antisense oligonucleotides id dermal fibroblasts," *Faseb J.* (1995) 9:1371-1377. | |
| | FK | LIN, K.-Y. et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," *J. Am. Chem. Soc.* (1998) 120(33):8531-8532. | |
| | FL | LIPARDI, C. et al., "RNAi as Random Degradative PCR: siRNA Primers Convert mRNA into dsRNAs that Are Degraded to Generate New siRNAs," *Cell* (2001) 107:297-307. | |
| | FM | LIU, K. et al., "Efficient Nuclear Delivery of Antisense Oligodeoxynucleotides and Selective Inhibition of CETP Expression by Apo E Peptide in a Human CETP-Stably Transfected CHO Cell Line," *Arterioscler. Thromb. Vasc. Biol.* (1999) 19:2207-2213. | |
| | FN | LIXIN, R. et al., "Novel Properties of the Nucleolar Targeting Signal of Human Angiogenin," *Biochem. Biophys. Res. Comm.* (2001) 284:185-193. | |
| | FO | LUKHTANOV, E. A. et al., "Direct, Solid Phase Assembly of Dihydropyrroloindole Peptides with Conjugated Oligonucleotides," *Bioconjugate Chem.* (1996) 7(5):564-567. | |
| | FP | MANOHARAN, M., "Oligonucleotide Conjugates in Antisense Technology," *Antisense Drug Technology, Principles, Strategies, and Applications*, Crooke, S. T. ed., Marcel Dekker, New York, (2001) Chapter 16, 391-467. | |
| | FQ | MANOHARAN, M. et al., "Novel Functionalization of the Sugar Moiety of Nucleic Acids for Multiple Labeling in the Minor Groove," *Tetrahedron Letters* (1991) 32(49):7171-7174. | |

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Sheet 10 of 13

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| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
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|---|---|---|---|
| | FR | MANOHARAN, M., "Oligonucleotide Conjugates as Potential Antisense Drugs with Improved Uptake, Biodistribution, Targeted Delivery and Mechanism of Action," *Antisense & Nucleic Acid Drug Development* (2002) 12:103-128. | |
| | FS | MANOHARAN, M., "Designer Antisense Oligonucleotides: Conjugation Chemistry and Functionality Placement," *Antisense Research and Applications*, Crooke and Lebleu, eds., CRC Press Boca Raton, FL (1993) Chapter 17, 303-349. | |
| | FT | MANOHARAN, M. et al., "Lipidic Nucleic Acids," *Tetrahedron Lett.* (1995) 36(21):3651-3654. | |
| | FU | MARTINEZ, J. et al., "Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi," *Cell* (2002) 110:563-574. | |
| | FV | MARUENDA, H. et al., "Antisense Sequence-Directed Cross-Linking of DNA Oligonucleotides by Mitomycin C," *Bioconjugate Chem.* (1996) 7(5):541-544. | |
| | FW | MARUENDA, H. et al., "Antisense sequence-directed cross-linking of RNA oligonucleotides by mitomycin," *Anti-Cancer Drug. Des.* (1997) 12:473-479. | |
| | FX | MELLITZER, G. et al., "Spatial and temporal 'knock down' of gene expression by electroporation of double-stranded RNA and morpholinos into early postimplantation mouse embryos," *Mechanisms of Development* (2002) 118:57-63. | |
| | FY | MEUNIER, L. et al., "The nuclear export signal-dependent localization of oligonucleopeptides enhances the inhibition of the protein expression from a gene transcribed in cytosol," *Nucleic Acids Res.* (1999) 27(13):2730-2736. | |
| | FZ | MILI, S. et al., "Distinct RNP Complexes of Shuttling hnRNP Proteins with Pre-mRNA and mRNA: Candidate Intermediates in Formation and Export of mRNA," *Mol. Cell Biol.* (2001) 21(21):7307-7319. | |
| | GA | MISHRA, R. K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-mediated delivery," *Biochim. Biophys Acta.* (1995) 1264:229-237. | |
| | GB | MONTGOMERY, M. K. et al., "RNA as a target of double-stranded RNA-mediated genetic interference in *Caenorhabditis elegans*," *Proc. Natl. Acad. Sci. USA* (1998) 95:15502-15507. | |

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Sheet 11 of 13

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| *Application Number* | 10/700,971 |
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| *First Named Inventor* | Muthiah Manoharan |
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|---|---|---|---|
| | GC | NAPOLI, C. et al., "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes *in trans*," *Plant Cell* (1990) 2:279-289. | |
| | GD | NELSON, P. S. et al., "Bifunctional oligonucleotide probes synthesized using a novel CPG support are able to detect single base pair mutations," *Nucleic Acids Res.* (1989) 17(18):7187-7194. | |
| | GE | NISHIKURA, K. et al., "A Short Primer on RNAi: RNA-Directed RNA Polymerase Acts as a Key Catalyst," *Cell* (2001) 107:415-418. | |
| | GF | OBERHAUSER, B. et al., "Effective incorporation of 2'-O-methyl-oligoribonucleotides into liposomes and enhanced cell association through modification with thiocholesterol," *Nucleic Acids. Res.* (1992) 20(3):533-538. | |
| | GG | PARRISH, S. et al., "Functional Anatomy of a dsRNA Trigger: Differential Requirement for the Two Trigger Strands in RNA Interference," *Molecular Cell* (2000) 6:1077-1087. | |
| | GH | PICHON, C. et al., "Intracellular Routing and Inhibitory Activity of Oligonucleopeptides Containing a KDEL Motif," *Mol. Pharmacol.* (1997) 51:431-438. | |
| | GI | PRAKASH, T. P. et al., "Synthesis of Site-Specific Oligonucleotide-Polyamine Conjugates," *Bioorg. Med. Chem. Lett.* (1994) 4(14):1733-1738. | |
| | GJ | RAJUR, S. B. et al., "Covalent Protein-Oligonucleotide Conjugates for Efficient Delivery of Antisense Molecules," *Bioconjugate Chem.* (1997) 8(6):935-940. | |
| | GK | RHODES, J. et al., "Therapeutic potentiation of the immune system by costimulatory Schiff-base-forming drugs," *Nature* (1995) 377(6544):71-75. | |
| | GL | RUMP, E. T. et al., "Preparation of Conjugates of Oligodeoxynucleotides and Lipid Structures and Their Interaction with Low-Density Lipoprotein," *Bioconjugate Chem.* (1998) 9(3):341-349. | |
| | GM | SAISON-BEHMOARAS, T. et al., "Short modified antisense oligonucleotides directed against Ha-*ras* point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation," *EMBO J.* (1991) 10(5):1111-1118. | |

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Sheet 12 of 13

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| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
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|---|---|---|---|
| | GN | SCHWARZ, D. S. et al., "Evidence that siRNAs Function as Guides, Not Primers, in the *Drosophila* and Human RNAi Pathways," *Molecular Cell* (2002) 10:537-548. | |
| | GO | SHEA, R. G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates," *Nucleic Acids Res.* (1990) 18(13):3777-3783. | |
| | GP | SIJEN, T. et al., "On the Role of RNA Amplification in dsRNA-Triggered Gene Silencing," *Cell* (2001) 107:465-476. | |
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Sheet 13 of 13

| Complete if Known | |
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| Application Number | 10/700,971 |
| Filing Date | November 4, 2003 |
| First Named Inventor | Muthiah Manoharan |
| Art Unit | 1623 |
| Examiner Name | To Be Determined |
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| Examiner Initials * | Cite No.[1] | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T[2] |
|---|---|---|---|
| | GY | WANG, X. et al., "Modular Recognition of RNA by a Human Pumilio-Homology Domain," *Cell* (2002) 110:501-512. | |
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